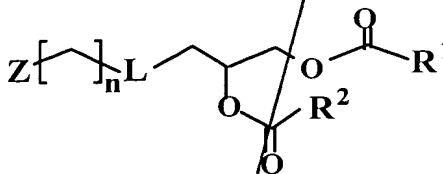


IT IS CLAIMED:

1. A liposome composition comprising:
a lipid having the formula



wherein each of R^1 and R^2 is an alkyl or alkenyl chain having between about 8 to about 24 carbon atoms;

$n = 1-20$;

L is selected from the group consisting of: (i) $-\text{X}-(\text{C}=\text{O})-\text{Y}-\text{CH}_2-$, (ii) $-\text{X}-(\text{C}=\text{O})-$, and (iii) $-\text{X}-\text{CH}_2-$, wherein X and Y are independently selected from oxygen, NH, and a direct bond;

Z is a weakly basic moiety that has a pK of less than about 7.4 and greater than about 4.0.

2. The composition of claim 1, wherein X is NH and Y is oxygen.

3. The composition of claim 1, wherein L is a carbamate linkage, an ester linkage or a carbonate linkage.

4. The composition of claim 1, wherein L is $\text{NH}-(\text{C}=\text{O})-\text{O}-\text{CH}_2$.

5. The composition of claim 1, wherein Z is an imidazole.

6. The composition of claim 1, comprising between about 1 to about 80 mole percent of the lipid.

7. The composition of claim 1, wherein Z is a moiety having a pK value between about 5.0 to about 6.5.

000001-0166.30

Sub
A7

8. The composition of claim 1, wherein each of R^1 and R^2 is an unbranched alkyl or alkenyl chain having between about 8 to about 24 carbon atoms.

9. The composition of claim 8, wherein each of R^1 and R^2 is $C_{17}H_{35}$.

5

10. The composition of claim 1, wherein n is between 1-10.

11. The composition of claim 1, further comprising a therapeutic compound entrapped in the liposomes.

10

12. The composition of claim 11, wherein the therapeutic agent is a nucleic acid.

15

13. The composition of claim 12, wherein the nucleic acid is selected from the group consisting of DNA, RNA, and their complements.

14. The composition of claim 1, further comprising a ligand for targeting the liposomes to a target site.

20

15. The composition of claim 14, wherein the ligand has binding affinity for endothelial tumor cells and is internalized by the cells.

25

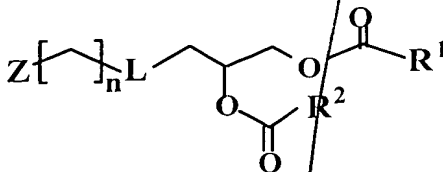
16. The composition of claim 15, wherein the ligand is selected from the group consisting of E-selectin, Her-2, and FGF.

17. The composition of claim 1, wherein the liposomes further comprise between about 5 to about 20 mole percent of a vesicle-forming lipid derivatized with a hydrophilic polymer chain.

30

18. The composition of claim 17, wherein the hydrophilic polymer chain is polyethyleneglycol (PEG).

19. A lipid having the formula:



wherein each of R^1 and R^2 is an alkyl or alkenyl chain having between about 8 to about 24 carbon atoms;

5 $n = 1-20$;

L is selected from the group consisting of (i) $-X-(C=O)-Y-CH_2-$, (ii) $-X-(C=O)-$, and (iii) $-X-CH_2-$, wherein X and Y are independently selected from oxygen, NH and a direct bond; and

10 Z is a weakly basic moiety that has a pK of less than about 7.4 and greater than about 4.0.

20. The lipid of claim 19, wherein X is NH and Y is oxygen.

15 21. The lipid of claim 19, wherein L is a carbamate linkage, an ester linkage or a carbonate linkage.

22. The lipid of claim 19, wherein L is $NH-(C=O)-O-CH_2$.

20 23. The lipid of claim 22, wherein Z is an imidazole.

24. The lipid of claim 19, wherein Z is a moiety having a pK value between about 5.0 to about 6.5.

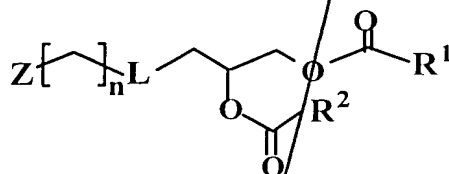
25 25. The lipid of claim 19, wherein each of R^1 and R^2 is an unbranched alkyl or alkenyl chain having between about 8 to about 24 carbon atoms.

26. The lipid of claim 23, wherein each of R^1 and R^2 is $C_{17}H_{35}$.

27. The lipid of claim 19, wherein n is between 1-10.

5

5



10

n = 1-20;

L is selected from the group consisting of (i) $-X-(C=O)-Y-CH_2-$, (ii) $-X-(C=O)-$, and (iii) $-X-CH_2-$, wherein X and Y are independently selected from oxygen, NH, and a direct bond;

15

administering the liposomes to the subject.

20

32. The method of claim 31 wherein the nucleic acid is DNA, RNA, or their complements.

25

entrapping a protein or a protein/fragment in the liposomes.